REMARKS/ARGUMENTS

This communication responds to the Office Action of April 10, 2008, in which claims 14, 15, 18-20, 22, 23, 32-34, 36-43 and 45-51 are pending.

CLAIM REJECTIONS UNDER 35 USC § 103

Claims 14, 15, 18-20, 22, 23, 32-34, 36-43 and 45-51 are being rejected to under 35 USC § 103 as being unpatentable over Erwin (U.S. 2005/0025756) in view of Soft Gel Technologies, Inc. (EP 888 774) and Davidson et al. (US 2004/0001874).

The rejection is overcome, at least, for the following reasons.

Erwin Is Not Prior Art

First, Applicant points out that the Office's rejection of the inventors § 1.131 declaration is in error. Specifically, the Erwin provisional application has a filing date of June 25, 2003. In his declaration, Michael Fantuzzi states, **and provides copious evidence** that the instant invention was conceived at least as early as March 13, 2003. Further, in the declaration the inventor has provided original emails, notebook pages and real data showing that, following conception, the inventor diligently reduced the invention to practice, showing the solubilization of CoQ10 in limonene by March 13, 2003 including its encapsulation in soft gelatin capsules. This utility application, fully enabled and containing actual experimental data was filed having a date of September 29, 2003.

With respect to Erwin, applicants note that the Erwin provisional application never suggests the encapsulation of a solution of CoQ10 in a soft gel capsule. Erwin merely suggest, without data or evidence, that CoQ10 may be soluble in limonene.

The Requirements Of 37 CFR § 1.131 Have Been Met

In addition, in the previous office action, one of the Office's reasons for rejecting the inventor's § 1.131 declaration was that the declaration only described the reduction to practice of the limonene/CoQ10 solution and not the encapsulation of the solution in a soft gelatin capsule. This is incorrect. The September 27, 2007 declaration specifically states that one purpose of the

research was to "determine solubility, optimum ranges and any other co-constituents that may be desirable ***in a soft-gel capsule***." Declaration at page 1 (emphasis added). Further, in order to make absolutely clear that inclusion of the limonene/CoQ-10 solution in a soft gel capsule was contemplated at the beginning of the inventor studies, the inventor submitted a second declaration to the Office on February 12, 2008. In the February 12, 2008 declaration, the inventor states categorically that the reduction to practice of dissolving CoQ-10 in limonene and the encapsulation of the solution provided thereby are one and the same. That is, because one of the focal priorities of Soft Gel Technologies is to provide constituents in a soft-gel capsule, the inventor had already identified that the composition comprising a solution of CoQ-10 in limonene would be encapsulated in a soft gel capsule. Moreover, this purpose is recited in the September 27, 2007 declaration. In addition, the as-filed claims of the instant application specifically recite that the invention comprises a solution of CoQ-10 in a monoterpene solution (claim 1); where that monoterpene is limonene (claim 3); and where the solution is contained in a soft gelatin tablet (claim 6). In addition, the Office's attention is directed to page 144 of Mr. Fantuzzi's notebook provided with the declaration where Mr. Fantuzzi notes that he added oil to the CoQ-10/limonene solution because in some instances adding pure limonene to a soft gel capsule was not real practical "although we do make such a product." Thus the declaration does state that the preparation of a limonene filled soft gel had been made.

Thus, as is required by MPEP 2138.05, the inventor shows by prior conception and reduction to practice, before the filing date of the Erwin application, that he was in possession of the invention and this culminates with the actual filing of the application. Thus, for this reason alone, Erwin is not prior art to the instant invention. The § 103 rejection over Erwin is therefore overcome and cannot stand.

The Office Is Not Free to Disregard 37 CFR § 1.131

37 CFR § 1.131 requires that the declaration establish reduction to practice prior to the effective date of the Office's cited art, or conception of the invention prior to the effective date of the reference coupled with due diligence from prior to the said date to a subsequent reduction to practice or to the filing of the application. This is exactly what the Michael Fantuzzi's declaration has provided. In fact, as discussed below, the Fantuzzi declaration shows conception

and reduction to practice before any conception or reduction to practice by Charles Erwin. The declaration is based on facts, provides specific dates and data from the inventor's notebook and provides contemporaneous corroboration via multiple email communication evidencing the veracity of everything stated in the declaration. The Office is not free to disregard the declaration as discussed below. ***There is no deficiency in the Fantuzzi declaration***.

The Requirements of MPEP 715 Have Been Met

MPEP 715.07 Requires that the Office Consider the Declaration in its entirety. "***The essential thing to be shown under 37 CFR 1.131 is priority of invention and this may be done by any satisfactory evidence of the fact.***" MPEP 715.07. "37 CFR 1.131(b) requires that original exhibits of drawings or records, or photocopies thereof, accompany and form part of the affidavit or declaration or their absence satisfactorily explained. . . . when reviewing a 37 CFR 1.131 affidavit or declaration, the examiner ***must*** consider all of the evidence presented in its entirety, including the affidavits or declarations and all accompanying exhibits, records and "notes." *An accompanying exhibit need not support all claimed limitations, provided that any missing limitations is supported by the declaration itself.* Ex parte Ovshinsky, 10 USPQ2d 1075 (Bd. Pat App. & Inter. 1989). Id. (emphasis added). Therefore, Applicant submits that the rejection of the inventor's declaration is in error both as judged by the verbatim requirements of 37 CFR § 1.131 and as required by the instruction for examination provided for the Examiner in MPEP 715.07. Thus, for this reason, the rejection over Erwin is overcome and must be withdrawn. Applicants respectfully request same.

Erwin is not enabled

MPEP 2121 Requires That The Prior Art Cited Be Enabled

In "determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure' . . . *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968). The disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation." MPEP 2121.01. In the instant case, provisional application 60/462,781 provides no enabling disclosure of the solubility

of CoQ-10 in limonene. The priority date of Erwin is based on a filing date of a provisional application which is not enabled. The single example is entirely prophetic and does not provide any evidence that the CoQ-10 will actually dissolve in the limonene. The Examiner is further referred to MPEP 2121.02 (I)

> Where a process for making the compound is not developed until after the date of invention, the mere naming of a compound in a reference, without more, cannot constitute a description of the compound. *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968). Note, however, that a reference is presumed operable until applicant provides facts rebutting the presumption of *>operability<. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). Therefore, applicant must provide evidence showing that a process for making was not known at the time of the invention. See the following paragraph for the evidentiary standard to be applied.

Erwin Was Not In Possession Of The Invention At The Time The Invention Was Made

The fact that Erwin is entirely prophetic and that Erwin was not in possession of the invention is evidenced by the fact that *Erwin requires that the limonene/CoQ-10 mixture be heated to 42°C* while continuously stirring the mixture. See, U.S. Provisional application 60/482,781 at 3. In contrast, the notebook pages from Mr. Fantuzzi, as well as the as-filed application, explicitly state that the solubilization of CoQ-10 in limonene occurs at room temperature, e.g., approximately 22°C. In fact, Mr. Fantuzzi's declaration identifies this unanticipated result with some degree of surprise. The Office is referred to the March 14, 2003 4:11 email provided to the Office in the inventors declaration. This result is illustrates a considerable difference from that *hypothetically* stated by Erwin. Further, Mr. Fantuzzi's results not only illustrate a greater utility of the Fantuzzi invention (e.g. not needing to heat the mixture with continuous stirring) but also could actually be determinative of the efficacy of the solution if the activity of CoQ-10 is harmed. This would be a real concern with the Erwin disclosure because the melting point of CoQ-10 is between 48 and 50 °C (see, APPENDIX I). The invention of Fantuzzi removes any doubt that the active ingredient – CoQ-10 could be harmed by higher than optimal temperatures required in solubilizing the CoQ-10. Thus, Erwin is not enabled and was not in possession of the invention at the time of the filing of the U.S. 60/482,781 provisional application because ***had Erwin been in possession of the knowledge of making a solution of CoQ-10 in limonene, Erwin would have known that it is not necessary to heat the mixture in order to solubilize the CoQ-10 in limonene.*** Not only is heating the mixture

to 42°C unnecessary, it has the potential to harm the beneficial and protective qualities of CoQ-10.

Further evidence of the prophetic and non-enabling disclosure of Erwin is provided by the fact that the Erwin only discusses being able to make a 25% solution of CoQ-10 in limonene, even with heating! In contrast, the Fantuzzi declaration states that the inventor was easily able to make a 40% solution with stirring for only 2-3 minutes by hand. Further, the declaration states that Mr. Fantuzzi could have made a more concentrated solution if he had desired to. This is attested by the as-filed specification itself where the inventor states that it is possible to get up to about 60% solubilization. In short, the Erwin provisional application is self evidence that Erwin was not in possession of the invention even by the, comparatively, late date of the filing of the provisional application.

Therefore, Erwin was not in possession of the invention, Erwin is not enabled and does not constitute prior art for the instant invention. The requirements of 2121.01 and 2121.02 having been further fulfilled. The Erwin provisional application comprises no more than "mere naming" and description of the subject matter. The rejection over Erwin being yet again overcome, the rejection should be withdrawn. Applicant, respectfully requests same.

Erwin Is Evidence That The Present Invention Is Novel And Non-Obvious

However, what Erwin does provide is further documentation and evidence that, prior to the present invention, the difficulty in solubilizing Co-Q10 was a problem well recognized by those of skill the art. For example, Weiss (previously provided to the Office in the IDS) and others performed a study comparing the four most prevalent oral forms of CoQ-10. This study compares the bioavialability of a hard gelatin capsule containing (1) 100mg of CoQ-10 and emcompress ®; (2) a soft gelatin capsule containing 100 mg of CoQ-10 and 400mg soy bean oil (Bioquinone ®); (3) a soft gelatin capsule containing 100 mg of CoQ-10 with 20 mg of PS 80, 100 mg of PTC and 280 mg of soy bean oil; and (4) a soft gelatin capsule containing 100 mg of CoQ-10 with 20mg of PS 80 and 380 mg of soy bean oil. Specifically, all of the supplements of CoQ-10 identified as being the most advantageous in the art at the time provided *no more than a 20% CoQ-10 compositions* ***in the form of a suspension***. Weiss at s274. In contrast, the present invention is capable of providing up to 60% concentrations of CoQ-10 without heating of the

solution. 10/674,268 at [0017]. The reason for this extraordinary difference is further explicitly provided in the as-filed application because the instant invention provide a ***solution***, **not a *suspension***. Moreover, **Weiss explicitly identifies that CoQ-10 is not soluble in soy bean oil**. Weiss states "The LSD analysis showed that only formulation no. 2 *(the soybean oil **suspension**)* could be distinguished significantly from the other formulations." Weiss at 277. That CoQ-10 was recognized as insoluble by those of skill in the art at the time the invention was made is further demonstrated by Folkers (U.S. Patent 4824,669), one of the pioneers in the field of CoQ-10 research. "Coenzyme Q10, being highly hydrophobic, is essentially insoluble in aqueous solutions." Folkers, col. 2, lines 3-5. In fact, the '669 patent is entirely directed to methods to obtain a homogenous composition of CoQ-10 which could be injected as there had not been identified a method of making a CoQ-10 solution. Therefore, Folkers teaches a "CoQ10 formulation . . . consists essentially of a clinically accepted ***fatty emulsion*** having an oil phase and a coenzyme Q10 dissolved in the oil phase. . . . the formulation preferably contains coenzyme Q10 at a level between about 7.5 μg/ml and about 30 ug/ml." Folkers, col. 3, lines 5-8. This provides a composition of only about 0.00075% to about 0.0030 %. Clearly, as stated by Folkers, the problem with oil phase composition is that they provide only ***emulsions*** and *Folkers could not identify a means of providing CoQ-10 in a solution. If Folkers had identified a way to provide a solution of CoQ-10, applicant submits, he would in fact, have stated so*. Further, for clarity sake, applicants provide herewith the definition of emulsion.

> **emulsion.** Compare with colloid.
> A colloid formed from tiny liquid droplets suspended in another, immiscible liquid. Milk is an example of an emulsion.
> **colloid.**
> A colloid is a heterogeneous mixture composed of tiny particles suspended in another material. The particles are larger than molecules but less than 1 μm in diameter. Particles this small do not settle out and pass right through filter paper. Milk is an example of a colloid. The particles can be solid, tiny droplets of liquid, or tiny bubbles of gas; the suspending medium can be a solid, liquid, or gas (although gas-gas colloids aren't possible).

In contrast solution is defined as:

> **solution.**
> All molecules in an "ideal solution" interact in exactly the same way; the solvent-solvent, solvent-solute, and solute-solute intermolecular forces are all equivalent. Ideal solutions obey Raoult's law exactly.
> **homogeneous mixture. solution.** Compare with heterogeneous mixture, element and compound. A sample of matter consisting of more than one pure substance with properties that do not vary within the sample.

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Therefore, applicant submits that those of skill in the art at the time the invention was made had not identified a solvent acceptable for making a solution of CoQ-10. It was not until the present invention was made that it was recognized that limonene could comprise a solvent for CoQ-10. Therefore, for this reason alone, the rejection is overcome and should be withdrawn.

EP 888 774 Does not Teach the Present invention

As discussed above, the instant claims require a soft gelatin capsule comprising CoQ-10 solubilized in limonene. EP888 774 does not disclose a soft gelatin capsule comprising CoQ-10 solubilized in limonene. As with other prior literature describing CoQ-10, the '774 document discusses the problem of providing a bioavailable composition containing CoQ-10. The '774 document provides a method of increasing the bioavailability of CoQ-10. Therefore, the '774 document describes a formulation including rice bran oil and vitamin E in addition to CoQ-10 and its encapsulation in a soft gelatin capsule. This product acts to provide a greater bioavailable amount of CoQ-10 by increasing the intestinal absorption through the inclusion of the vitamin E. See, '774 page 2, lines 5-8. The '774 document never mentions limonene, nor even mentions identifying media in which to "solubilize" CoQ-10. The '774 document is limited to a composition comprising CoQ-10 with rice bran oil and vitamin E. In short, the '774 document neither makes the instant invention obvious nor anticipates it. The rejection over EP888 774 is therefore overcome and should be withdrawn. Applicant respectfully requests same.

Davidson Does Not Remedy The Defects Of EP888 774

Davidson discusses, generally, "methods for identifying and developing safe and effective nutritional supplemental formulations." (Abstract). These methods are illustrated in, for example, Fig. 1. This figure illustrates the collection of studies pertaining to health risks, identifying nutritional supplements having positive impact, reviewing the studies, eliminating nutritional supplements, combining remaining nutritional supplements, and select optimum delivery mechanisms. Davidson contains only a single paragraph regarding CoQ-10. "it is possible to ***blend*** co-enzyme Q10 (also known as ubiquinone) within the fish oil capsule to reduce the amount of fish oil needed by the patient in each packet." Davidson at [0057] (emphasis added). Davidson contains no mention of limonene. Davidson explicitly does not teach that CoQ-10 is soluble in anything. In addition, "blend" does not equate with solubilize or

dissolve. Specifically, when used as a verb, blend has the meaning "to mix or combine together." In a chemical sense, blending is antithetical to making a solution because if one made a solution then Davidson would use the term "dissolve". Blending would not be used by one of skill in the art to describe the making of a solution. Therefore, Davison, lacking the elements of the present invention, namely limonene, a solution of CoQ-10 and, further, a solution of CoQ-10 in limonene, cannot make obvious or anticipate the present invention. The rejection over Davidson is overcome and should be withdrawn.

***In Re Kerkhoven* Requires That A Combination Of Compositions Contain All The Ingredients Of The Combination**

"It is impermissible with the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art." *In re Wesslau*, 353 F.2d at 241, (Fed. Cir. 1965). This admonition from the Federal Circuit was reinforced in Kerkhoven, when the court taught "it is prima facie obvious to combine two compositions, each of which is taught by the prior art, to be useful for the same purpose in order to form a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art." Thus, according to *In re Kerkhoven*, and as further reinforced in *Wesslau*, when the Office combines art to make a rejection, the result should be the combination of the compositions. In the case of the above rejection, EP888 774 requires, at least, rice bran oil and vitamin E. Davidson, while describing only a method for identifying nutraceuticals, provides a long list of potential nutraceuticals, which it describes in much greater detail than the mention of CoQ-10.

Therefore, the combination of the art cited by the Office would not yield the present invention. First, the combination would lack limonene. Second, the combination would have, at least, rice bran oil, vitamin E, EPA, DHA, folic acid, B6 vitamins, B12 vitamins, niacin, plant sterols . . . and the remaining 26 elements listed in Table 2 of Davidson. Therefore, for this reason alone, the rejection over Davidson is overcome and should be withdrawn. Applicant respectfully requests same.

Finally, applicant notes that the Office has combined multiple references to extract the components of the instant invention. In this context, applicant notes that even if Erwin was prior art, which it categorically is not, it would not help the Examiner's case. First, the instant invention teaches that a solution can be made with CoQ-10 in limonene at room temperature. Erwin states that the mixture must be heated to 42°C with constant stirring. Further, Erwin includes numerous other agents that are not necessary for the present invention. In addition, combining the ingredients of the 888 774 application further require the addition of other ingredients not required by the instant invention. Davidson requires the addition of yet further ingredients in his "method" for identifying supplement formulations – all of which would surely require the identification of some completely exotic solvent to get all the ingredients in solution. Therefore, for this reason alone the Examiners rejection is in error and should be withdrawn.

The Rejection Is The Result Of Hindsight Reconstruction

The fact that the Office has had to cobble together multiple documents, which are internally incompatible with each other in order to identify as obvious the instant invention and to deny the inventors § 1.131 declaration illustrates that the rejection is based on hindsight reconstruction. Courts have repeatedly warned that the patentability of an invention is not to be viewed with hindsight or "viewed after the event." See Goodyear Co. v. Ray-O-Vac Co., 321 U.S. 275, 279, 64 S.Ct. 593, 88 L.Ed. 721 (1944) and authorities cited therein. The Office is further reminded of the warning recently provided by the Supreme Court and as further cited by the Board of Patent Appeals. "[A] factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of argument reliant upon ex post reasoning." KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727 at 1742. The rejection over Erwin, 888774 and Davidson has been overcome. Withdrawal is respectfully requested.

The Art Cited By The Office Is Evidence Of A Long Felt Need By Those Of Skill

Throughout the prosecution of this application as well as its sister applications (which arose out of an Office imposed restriction) the Office has cited multiple articles and patents that describe various methods of making CoQ-10 supplements. All of the art cited discusses the desirability of such supplements and difficulty in making such supplements due to the very low solubility of CoQ-10. Such articles include the Folkers patent, for example, which teaches the

need for making micro-emulsions of CoQ-10, Kommuru (previously provided to the Office), Davidson, the Garti patent, the '774 document and Erwin itself. Further, the Offices attention is directed to U.S. patent 7,026,361 to Minemura et al. which further discusses this difficulty and finds an answer by melting the CoQ-10 to then dispersing the CoQ-10 in a liquid in the presence of an organic acid to forma protective colloid. This time consuming process only yields up to a 25 % and preferably a 7 % preparation. Thus, were the invention obvious, were any of the art suggestive of the instant invention, it would have been made prior to the making of the invention by Michael Fantuzzi. The fact that none of the art cited by the Office suggests the ability to make any more that a 5% solution in oil, that the art cited by the Office which does profess to make a greater amount of CoQ-10 available resorts to emulsions or nano-sized carriers is testament to the fact that the instant invention is novel and non-obvious and that those of skill in the art have attempted many methods of identifying a way to solubilize and make more CoQ-10 available in a nutraceutical formulation. Michael Fantuzzi was the first to identify limonene as the solution to this problem. The rejections being now overcome, allowance of the claims is respectfully requested.

CONCLUSION

This response is being submitted on or before October 10, 2008, with the required fee for a 3-month extension of time, making this a timely response. It is believe that no additional fees are due in connection with this filing. However, the Commissioner is authorized to charge any additional fees, including extension fees or other relief which may be required, or credit any overpayment and notify us of same, to Deposit Account No. 04-1420.

This application now stands in allowable form and reconsideration and allowance is respectfully requested.

Respectfully submitted,

DORSEY & WHITNEY LLP
Customer Number 25763

Date: Sept. 22, 2008

By: _____
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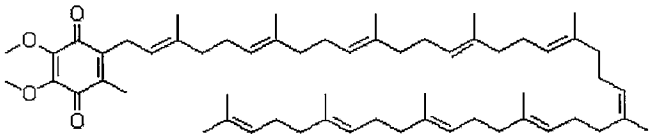
APPENDIX I

Ubidecarenone

Identification

Name	Ubidecarenone
Synonyms	Ubiquinone 10; Coenzyme Q10
Molecular Structure	
Molecular Formula	$C_{59}H_{90}O_4$
Molecular Weight	863.36
CAS Registry Number	303-98-0
EINECS	206-147-9

Properties

Melting point	48-52 °C

Safety Data

Safety Description	S22;S24/25 Details

List of Suppliers

The Complete List of Suppliers for Ubidecarenone

Ubenimex Ufiprazole Ultraviolet Absorbent UV-1164 Ultraviolet Absorbent UV-360 Undecane 1,11-Undecanedicarboxylic acid Undecanedioic acid 1,11-Undecanediol Undecanoic acid Undecanolactone Undecan-4-olide 6-Undecanone 2-Undecanone Undecanoyl chloride 2-Undecenal Undecenoic acid Uniconazole Uracil Urapidil Urea Urea formaldehyde Urea hydrogen peroxide Urea phosphate Urethane 6,6'-Ureylene-bis(1-naphthol-3-sulfonic acid) Uridine Uridine 5'-diphosphoglucose disodium salt Uridine-5'-diphosphoglucose disodium salt Uridine-5'-triphosphoric acid trisodium salt Urocanic acid Urokinase Ursodeoxycholic acid Ursolic acid Ursolic acid acetate Ursonic acid benzyl ester (+)-Usniacin UV absorber-928